

Prolonged Low Doses of Methylprednisolone for Patients With COVID-19 Severe Acute Respiratory Syndrome

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MP-C19 Statistical analysis plan

Sample size calculation

The Chinese observational study published by Wu et al. in JAMA Intern Med on 03/13/2020 showed that the use of MP leads to a mortality reduction of about 15% (30-day mortality: 46.0% in 50 treated patients vs. 61.8 % in 34 untreated patients; survival median: 25 days vs. 10 days, HR 0.4, 95% CI: 0.2-0.7). Furthermore, the same study shows a proportion of ICU admissions of patients with ARDS of 63% and use of intubation and invasive VM in 79% of ARDS cases.

Given a study power (1-beta) of 80% and a probability of type 1 error (alpha) of 0.05, we calculated a sample size of 98 patients (49 for each group) using a 2-tailed, proportional Z-test (pooled). Considering the primary outcome, it is expected from the literature that a proportion equal to about 70% of patients with ARDS get intubated and/or hospitalized in ICU and/or die. We hypothesize that this proportion could be reduced by at least 40% with the MP-based intervention in the respiratory high-dependency unit setting. Considering a 5% dropout rate, a total of minimum 104 patients will need to be enrolled (52 per group).

Statistical analysis plan

The data will be described using absolute and relative frequencies (expressed as a percentage) or position indices (average or median) and relative dispersion indices (standard deviation or interquartile range) suitable for the type of variable analysed.

As for the primary outcome, the differences between the study groups (treated vs. controls) will be assessed using a test for proportions (e.g. Z-test), considering statistically significant a p-value <0.05.

With regards to the secondary outcomes, the differences between the study groups in the continuous variables will be evaluated with the t-test or with the Mann-Whitney test, depending on the distribution of the variables. The differences between the study groups regarding categorical or dichotomic variables (proportions) will be analysed with the Chi-square test or with the Fisher test, as more appropriate. For time-dependent variables (e.g. survival) analysis will be conducted with the Kaplan-Meier method and the differences between groups will be assessed with the log-rank test. If the number allows, subject to verification of the validity of the proportionality assumption, a multivariate analysis of Cox will be conducted to take into account potential confounders. A two-tailed test p-value of less than 0.05 will be considered statistically significant.

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